JACC Vol. 26, No. 4
October 1995:1016-21

Cardiopulmonary Function in Adult Patients Late After Fontan Repair

DAVID A. HARRISON, MD, FRCPC, PETER LIU, MD, FRCPC, FACC,
JANICE E. WALTERS, BScN, RN, JACK M. GOODMAN, PhD, SAMUEL C. SIU, MD, FRCPC, FACC,
GARY D. WEBB, MD, FRCPC, FACC, WILLIAM G. WILLIAMS, MD, FRCSC,
PETER R. McLAUGHLIN, MD, FRCPC, FACC

Toronto, Ontario, Canada

Objectives. **The clinical status and exercise assessment of adult patients late after the Fontan operation were reviewed to determine cardiovascular function.**

Background. **The Fontan operation is the final operation for many patients with tricuspid atresia or a single ventricle. Follow-up reports describe most patients to be in Canadian Cardiovascular Society functional class I or II. Objective measures of cardiac performance in the pediatric age group have shown significant dysfunction.**

Methods. **Forty-seven adult patients were seen late after the Fontan operation at the Toronto Congenital Cardiac Centre for Adults. Thirty of these underwent cycle ergometry to determine maximal exercise capacity. Maximal ventilation, maximal oxygen uptake and anaerobic threshold were determined from a ramp exercise protocol. Ejection fraction at rest and during exercise was measured with gated radionuclide angiography. Results were compared with those of eight normal volunteers. Results are given as mean ± SD.**

Results. **Thirty patients underwent cardiopulmonary exercise testing 6.7 ± 3.9 years after a first Fontan operation. Clinically 93% were in functional class I or II. The Fontan group patients had a significantly lower maximal work load (548 ± 171 vs. 1,094 ± 190 kilopond-meters, $p < 0.00001$), anaerobic threshold (11.2 ± 2.9 vs. 23.6 ± 4.6 ml/kg per min) and maximal oxygen consumption (14.8 ± 4.5 vs. 42.1 ± 10.0 ml/kg per min). Systemic ventricular ejection fraction was lower at rest (38 ± 12% vs. 58 ± 7%) and during exercise (40 ± 15% vs. 70 ± 8%).**

Conclusions. **Despite a clinical impression of good function, by objective measures adult patients continue to have significant cardiovascular limitation late after the Fontan operation.**

(J Am Coll Cardiol 1995;26:1016-21)

The Fontan procedure, which was developed for palliation of tricuspid atresia (1), is often the final surgical procedure for both tricuspid atresia and a univentricular heart. Postsurgical follow-up reports (2–8) have demonstrated extended survival accompanied by a certain degree of morbidity, mortality and reoperation. Despite reports of good clinical functional status in patients after Fontan repair, objective measures of ventricular function (9,10) and the response of patients to exercise (11–17) have shown significant limitation when compared with those of a normal population. However, the majority of patients undergoing the Fontan operation are in the pediatric age group at the time of operation. There is very little corresponding information in adults with the Fontan procedure. Early surgical reports (2,3) suggested that there is an increased surgical risk for patients <4 or >16 years old at time of operation. This concept has been superseded by recent reports of good surgical results in adult patients (5,6,18). Long-term postsurgical follow-up also suggested a possible deterioration in functional capacity in patients followed up for 10 to 15 years after operation (4). Therefore, information on the long-term follow-up of functional capacity in adult patients with the Fontan procedure is warranted.

In the present study we assessed a group of adult patients (≥18 years old) who had a previous Fontan procedure. We prospectively determined the subjective and objective measures of cardiopulmonary performance and ventricular function in these patients versus a group of age-matched control subjects.

Methods

Patients. Forty-seven patients with a previous Fontan operation have been followed at the Toronto Congenital Cardiac Centre for Adults since March 1989 (mean [±SD] age at follow-up 25.7 ± 6.3 years; 26 men, 21 women). The patients were seen an average of 6.7 ± 3.9 years after the initial Fontan

From the Toronto Congenital Cardiac Centre for Adults, Toronto Hospital, Centre for Cardiovascular Research, University of Toronto, Toronto, Ontario, Canada. This study was supported by a term grant from the Heart and Stroke Foundation of Ontario, Toronto, Ontario, Canada. Dr. Harrison is a research fellow, and Dr. Liu a Career Investigator, of the Heart and Stroke Foundation of Canada.

Manuscript received October 24, 1994; revised manuscript received April 28, 1995, accepted May 3, 1995.

Address for correspondence: Dr. Peter R. McLaughlin, Eaton Building 12-224, 200 Elizabeth Street, Toronto, Ontario, M5G 2C4, Canada.

0735-1097/95/$9.50
0735-1097(95)00242-V

operation. Mean age at the time of operation was 19.0 ± 7.8 years (range 8 to 40). The underlying anatomy included 25 patients with tricuspid atresia (19 with type I, 6 with type II). There were 22 patients with a univentricular connection (9 with double-inlet ventricle, 2 with double-inlet right ventricle, 2 with crisscross heart, 5 with complex forms of transposition, 4 with other forms of complex single ventricle). For patients with univentricular connections, the dominant ventricle was morphologically left in 15 patients and right in 7. At operation, 33 patients had a right atrial to pulmonary artery connection, only two of which included a valve in situ; 12 patients had a valved right atrial to subpulmonary ventricular connection; 2 patients with azygous continuation had a superior vena cava to pulmonary artery connection. Patients followed at the Toronto Congenital Cardiac Centre for Adults were enrolled in the follow-up program.

Eight age-matched sedentary male subjects (mean [±SD] 27.6 ± 3.5 years, range 24 to 33) formed the control group for comparison of exercise variables.

Follow-up program. *Clinical assessment.* Clinical assessment of all patients included history, physical examination and symptomatic status assessment according to Canadian Cardiovascular Society functional class (19), usually on a yearly basis. Patients underwent standard 24-h ambulatory electrocardiographic (ECG) monitoring using either Cardiodata PR3 or Oxford MR4 monitor systems. The majority of tapes were analyzed with Cardiodata Mark 4 system; a few tapes were analyzed with either the Oxford Excel or Marquette Electronics SXP Analysis System. Underlying rhythm, frequency of atrial and ventricular extrasystoles, presence of ventricular couplets and duration of nonsustained ventricular tachycardia, if present, were determined.

Cardiopulmonary exercise testing. Graded exercise using an electrically braked cycle ergometer was performed in the upright position to assess cardiopulmonary status. The patient's heart rate and rhythm were continuously monitored with a three-lead ECG. Blood pressure was measured by an automated cuff at 1-min intervals. Breath-by-breath collection of expired gases was obtained using a metabolic cart (Sensormedics 4400); results are reported as 15-s averages. Standard techniques were used to determine ventilatory volume during exercise.

After a 1-min warm-up phase against minimal resistance, the work load was increased continuously by 100 kilopondmeters (kpm) per min starting at 200 kpm. Exercise continued until a symptom-limited maximum was obtained. The ventilatory anaerobic threshold was determined by analysis of the expired gases. The threshold was determined as the breakpoint of the nonlinear increase in ventilation relative to increasing oxygen consumption and was verified by the point at which the ventilatory equivalent for oxygen increased without a corresponding increase in ventilatory equivalent for carbon dioxide.

Radionuclide ventriculography. Before initial exercise testing, the patient received red blood cell labeling with 20 mCi of technetium-99m pertechnetate using a standard modified in vivo technique. Gated radionuclide angiography (Apex 409 Elscint camera) was performed at rest in three views (anterior, lateral and best septal view individualized according to anatomy). To obtain exercise ventriculography, the patient underwent a second exercise protocol with warm-up of 1 min at 200 kpm, after which the exercise load was increased to 70% of the patient's previous maximal work load. Patients sustained exercise at this level for 2 min to attain steady state and an additional 1 min for nuclear data acquisition, measured in the previously determined best septal view. The ejection fraction was then analyzed by an experienced independent observer with commercially available software using background subtraction from an adjacent pulmonary area.

The study protocol was approved by The Toronto Hospital Human Ethics Committee.

Echocardiography. The majority of patients had echocardiograms recorded during the time course of the present study. Exact time of studies did not routinely correspond to the dates for cardiopulmonary assessment. Studies obtained within 1 year of the cardiopulmonary test were reviewed for systemic ventricular dimensions, wall thickness and systemic atrioventricular (AV) valve regurgitation. All measurements were obtained from the left parasternal long-axis view with the patient in the left lateral position. Valvular regurgitation was assessed semiquantitatively on the basis of color flow Doppler and pulsed Doppler analysis.

Data analysis. The Fontan and control groups were compared for exercise, pulmonary function and cardiopulmonary and radionuclide variables. Comparison of rest and exercise ejection fractions within the control or Fontan group was made using the paired *t* test. For comparisons of rates, the chi-square or Fisher exact test was used where appropriate. Stepwise multiple linear regression was used to determine potential independent predictors of objective measures of exercise performance. All analysis was obtained using SPSS for Windows version 6.0.1 (SPSS Inc.).

Results

Clinical outcome. Forty-seven patients have been followed at the Toronto Congenital Cardiac Centre for Adults since March 1989. Twenty-one patients were in functional class I, 22 in class II, 3 in class III and 1 in class IV. There have been three deaths late after initial Fontan operation during the 4.5-year follow-up period. The patient in functional class IV had tricuspid atresia with an atriopulmonary valved conduit. Twelve years after initial operation, she underwent reoperation for conduit obstruction. She died 3 days after operation. A second patient with a single ventricle developed mitral regurgitation and right atrial thrombus 7 years after initial operation and died during thrombectomy and valve replacement. The third patient had a complex form of tricuspid atresia with azygous continuation; he had developed severe arteriovenous malformations in his lungs, resulting in cyanosis and clubbing. He was considered inoperable and died out of hospital 10 years after his Fontan operation. Average age at time of death was

Table 1. Clinical Characteristics of 30 Patients With Cardiopulmonary Testing Compared With Those of All 47 With Fontan Repair

	Study Group (n = 30)	Total Fontan Repair Group (n = 47)	p Value
Male gender	18 (60%)	26 (55%)	0.69
Female gender	12 (40%)	21 (45%)	
Age at operation (yr)	20.0 ± 8.7	19.0 ± 7.8	
Age at follow-up (yr)	26.6 ± 6.6	25.7 ± 6.3	
Native anatomy			
Tricuspid atresia I	14 (47%)	19 (40%)	0.67
Tricuspid atresia II	5 (17%)	6 (13%)	
Univentricle	11 (37%)	22 (47%)	
Operation			
RA-PA	18 (60%)	31 (66%)	0.90
RA-PA valved	1 (3%)	2 (4%)	
RA-RV valved	10 (33%)	12 (26%)	
SVC-PA	1 (3%)	2 (4%)	

Data presented are mean value ± SD or number (%) of patients. PA = pulmonary artery; RA = right atrium; RV = right ventricle; SVC = superior vena cava.

Table 2. Comparison of Functional Class and Medication Use in Study and Total Fontan Repair Groups

	Study Group [no. (%) of pts]	Total Fontan Repair Group [no. (%) of pts]	p Value (Pearson chi-square)
CCS functional class			
I	13 (43%)	21 (45%)	0.88
II	15 (50%)	22 (47%)	
III	2 (7%)	3 (6%)	
IV	0	1 (2%)	
Medications			
None	9 (30%)	16 (34%)	
Diuretic drugs	4 (13%)	7 (15%)	
Digoxin	13 (43%)	19 (40%)	
Antiplatelet agents	8 (27%)	8 (17%)	
Anticoagulant agents	5 (17%)	6 (13%)	
Antiarrhythmic agents	4 (13%)	6 (13%)	
ACE inhibitor	1 (3%)	3 (6%)	
Other	10 (33%)	14 (30%)	

ACE = angiotensin-converting enzyme; pts = patients.

21.9 years, a mean of 9.7 years after the initial Fontan operation.

Late reoperation after initial Fontan was necessary in 10 of the 47 patients in our study group. Reason for reoperation was conduit obstruction in nine patients, and the remaining patient had developed a right atrial thrombus and significant AV regurgitation. Among the nine patients with conduit obstruction, eight had a valve within their conduit (seven with AV connections, one with valved right atrial to pulmonary artery connection). Reoperation was performed at a mean of 8.2 ± 2.8 years (range 3.6 to 12.3 years) after the initial Fontan operation. Two of these patients died after operation; three are now in functional class I and five in class II.

Of the total of 47 patients, 30 consented to the detailed follow-up protocol. The reason for refusal in the remaining 17 patients included geographic distance (6 patients), patient unwilling to cooperate (8 patients), attempting pregnancy (1 patient) and death before the scheduled tests (2 patients). Tables 1 and 2 compare the characteristics of the 30 patients who underwent cardiopulmonary testing with those of all 47 with Fontan repair. Overall, the age at operation, age at follow-up, type of anatomy, type of operation and functional class were completely comparable between the two groups. Therefore, there was no detectable inadvertent bias in the subgroup that underwent detailed testing.

Clinical assessment. The functional classes of patients who had cardiopulmonary testing are shown in Table 2. The majority of our patients had a relatively high subjective evaluation of their exercise capacity and thought that there was no major limitation to their activities.

Arrhythmias. During follow-up of the 47 patients, 29 did not have a documented history of clinically significant arrhythmia. One patient was receiving therapy for a remote history of ventricular tachycardia and atrial flutter and died during follow-up. One patient had complete heart block and was pacemaker dependent. Sixteen patients had clinically recognized atrial arrhythmias; 1 of these 16 presented with a transient ischemic attack, and 1 presented with heart failure. Four patients have required pacemakers for sick sinus syndrome. Six patients were receiving antiarrhythmia medication other than digoxin to control their atrial arrhythmia. Each of the three patients who died had a history of arrhythmia.

The 30 patients who underwent exercise testing also had 24-h ambulatory ECG monitoring. The predominant rhythm was sinus in 21 patients; 4 patients had either atrial flutter or fibrillation; 2 had ectopic atrial tachycardia; 1 had accelerated junctional tachycardia; and 2 patients were in a paced rhythm. Two patients in predominantly sinus rhythm had brief runs of atrial arrhythmia on 24-h monitoring. Three patients had an average of >30 ventricular premature beats/hour; an additional two patients had ventricular couplets. There was no documented ventricular tachycardia during monitoring.

Exercise capacity. The maximal work load attained by the Fontan group was significantly lower at 548 ± 171 kpm than at 1,094 ± 190 kpm in the control group ($p < 0.00001$). The Fontan group reached a mean maximal heart rate of 151 ± 24 beats/min, which was significantly lower than that of 178 ± 19 beats/min reached by the control group ($p < 0.01$).

As shown in Table 3, peak ventilation in the Fontan group was ~50% of the level in the control group. The anaerobic threshold and peak oxygen consumption during exercise were also compared; both of these measures were significantly lower in the Fontan patients. The anaerobic threshold was ~50%, and the peak oxygen consumption <50%, of the level measured in the control group.

Ventricular function. Systemic left ventricular ejection fraction at rest is shown in Figure 1. In the Fontan group the mean left ventricular ejection fraction was 38 ± 12%, which

Table 3. Cardiopulmonary Exercise Assessment of Patients With Fontan Repair Compared With Control Subjects

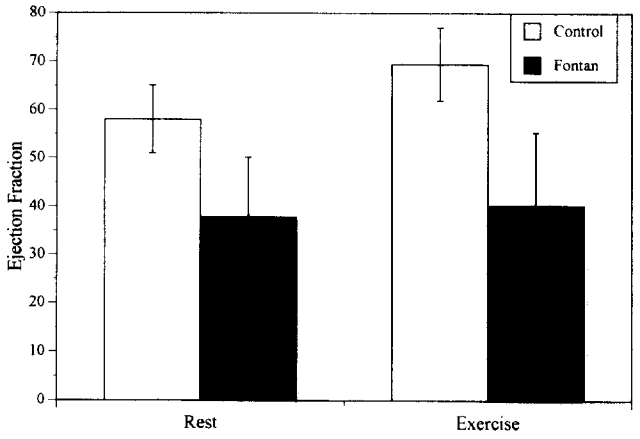
	Control Subjects (mean ± SD)	Fontan Repair (mean ± SD)	p Value
Maximal work load (kpm)	1,094 ± 190	548 ± 171	< 0.00001
Maximal ventilation (liters/min)	107 ± 17	57 ± 18	< 0.00001
Maximal oxygen consumption (ml/kg per min)	42.2 ± 10.0	14.8 ± 4.5	< 0.00001
Anaerobic threshold (ml/kg per min)	23.6 ± 4.6	11.2 ± 2.9	< 0.00001

kpm = kilopond-meters.

was significantly less than that in the control group (58 ± 7%, p = 0.0001). During exercise, ejection fraction in the Fontan group increased to 40 ± 15% (p < 0.05). In the control group ejection fraction increased during exercise to 70 ± 8% (p < 0.002). Ejection fraction during exercise remained significantly lower in the Fontan group than in the control group (p < 0.0001).

Echocardiographic assessment. Echocardiograms obtained within 1 year of the cardiopulmonary test were available for 26 patients. Systemic ventricular size in diastole was 54.7 ± 8.5 mm. Septal and posterior wall thicknesses were 10.4 ± 2.2 and 9.8 ± 1.2 mm, respectively. Atrioventricular valve regurgitation was judged to be moderate (2+) in three patients; the remaining 23 patients had no or mild regurgitation. Quantitative estimation of pulmonary pressures was not routinely attempted in this group of patients because of the multiple abnormalities and differing forms of surgical corrections of their venous ventricular connections.

Figure 1. Ventricular ejection fraction at rest and at peak exercise in control subjects and patients with the Fontan repair. Ejection fraction increased with exercise in both the Fontan (p < 0.05) and control (p < 0.002) groups. Ejection fraction in patients with the Fontan repair was significantly lower than that in the control group both at rest and during exercise (p < 0.0001). Data shown are mean value (**columns**) ± SD (**vertical bars**).



Subgroup analysis. We analyzed the cardiopulmonary data for possible differences between subgroups of the Fontan group. Stepwise multiple linear regression was used to model the following variables: work load, anaerobic threshold and maximal oxygen consumption as a function of gender, age at operation, time since operation, age at follow-up, ejection fraction at rest, underlying anatomy (tricuspid atresia vs. univentricular connection), surgical connection (atriopulmonary vs. AV) or previous Glenn operation. For maximal work load, patient gender was found to be a significant variable (600 ± 178 kpm for men, 470 ± 132 kpm for women, p < 0.05). There were no significant independent predictors for anaerobic threshold or maximal oxygen consumption.

Discussion

Summary of results. In the present study we reported the results of detailed cardiopulmonary testing in 30 patients late after Fontan operation. This group was drawn from a total of 47 patients with a Fontan procedure who are still followed at the Toronto Congenital Cardiac Centre for Adults. The majority of patients not included in the study either refused cardiopulmonary testing or lived a significant distance from our center and could not arrange to be available for exercise assessment. In the Fontan group there have been three deaths late after repair during 4.5 years of follow-up; two deaths were related to reoperation. Ten patients have required reoperation, nine for conduit obstruction and one for AV valve regurgitation. Sixteen patients have had documented atrial arrhythmias, six of whom required antiarrhythmic medication other than digoxin. Five patients are paced, one for complete heart block and four for sick sinus syndrome. Exercise testing has demonstrated significant limitations in cardiac function, with reduced ejection fraction at rest and during exercise accompanied by reduced anaerobic threshold and reduced oxygen consumption.

Previous studies of functional assessment. Previous reports of patient functional status are self-graded in terms of New York Heart Association functional class (2–4,7,18), sometimes by telephone and mail surveys of patients (5,6,8). The patients described in these reports have included all age groups, with the exception of one report (18) that focused on operation in the adult. All of the reports have uniformly described an excellent degree of functional capacity, with 80% to 93% of patients in class I or II. Although on average older than the patients described in these other reports, our patients also described high clinical function, with 91% of the adult Fontan group in functional class I or II.

Reports of good subjective clinical function are in distinct contrast to objective measures of exercise capacity. An early study of five patients after Fontan repair (mean age at operation 13.8 years) with class I function showed cardiac index and oxygen extraction to be significantly less than that in a control group (11). These findings have been confirmed in a separate

study obtained for another group of 18 patients in functional class I after Fontan repair (mean age at operation 12.5 years) (17). The group of 30 patients who had cardiopulmonary assessment at our center were representative of our total group of patients with a Fontan repair. This group clearly showed a significant reduction in maximal work load, anaerobic threshold and maximal oxygen consumption compared with a group of age-matched normal subjects. These levels of exercise performance and oxygen consumption are compatible with those found in patients with congestive heart failure (20). When the performance of our patients was compared with that of patients with heart failure, 5 patients were classified as having mild, 17 moderate and 4 severe heart failure. Clearly there is a vast discrepancy between the patient's and clinician's assessment of functional capacity versus objective cardiopulmonary testing. This discrepancy suggests that the subjective clinical assessments of our Fontan group are not sensitive to their cardiovascular limitations, probably because of the chronic nature of their cardiac condition and the lack of a normal "yardstick" for comparison in the patient's lifetime.

Mechanisms of functional limitation. A number of investigations have attempted to define the mechanism of cardiac response to exercise in the post-Fontan circulation. In our patients the heart rate at rest was normal and was seen to increase with exercise. However, peak heart rate in response to exercise was significantly reduced compared with that in the control group, suggesting a degree of chronotropic incompetence. This pattern of heart rate response to exercise has also been observed by others (14,15). Our exercise data showed an abnormal ejection fraction both at rest and with exercise. We measured ejection fraction at rest as 38 ± 12%. This estimate is less than the ejection fraction at rest measured by others using contrast angiography (range of reported mean values 50% to 66%) (2,11,21). Ejection fraction at rest measured by others using radionuclide angiography was 39% in a group of patients with a single ventricle (10) and ranged from 43% to 56% in three studies in patients with mixed anatomy (9,12,13). Because our patients were older than those in previous reports, it is possible that this trend to a lower ejection fraction may be caused by increasing age and the toll taken by long-term stress on the myocardium, leading to left ventricular dysfunction. However, we were unable to find a statistically significant effect of age on measured ejection fraction within our own patient group. Two centers have reported ejection fraction during exercise as measured by radionuclide angiography; both have demonstrated a small increase in ejection fraction with exercise (12,13). Our study in a larger group of patients also demonstrated a small but statistically significant increase in ejection fraction, from 38 ± 12% to 40 ± 15%.

The success of the Fontan operation is dependent on low systemic ventricular end-diastolic pressure, absence of systemic AV valve regurgitation and low pulmonary artery pressures (22). Of the patients with echocardiographic assessment of systemic AV valve function, only two had more than mild regurgitation. Ventricular end-diastolic pressure was not directly measured, and it is uncertain whether the Doppler patterns usually associated with left ventricular diastolic dysfunction or elevated left atrial pressure are reliable for estimating pressures in this patient cohort. Similarly, abnormal ventricular geometry limits the use of usual techniques for accurate estimation of left ventricular mass. Clearly, these features should be studied in more detail in the future.

Influence of age on cardiac function. Surgical reports of the Fontan operation in adults have been good (5,6,18), although risk of late mortality persists (7,8), with risk increasing at 6 years after operation (4). The deaths of 3 of our 47 patients confirm a continuing risk of death in this population. Influence of patient age on the outcome of the Fontan operation is also seen as a gradual shift from functional classes I and II to classes II and III (4). The average time since initial Fontan operation in our patients was 6.7 years. Despite this length of time, over 90% of our patients continue to report class I or II function.

In the 30 patients who had cardiopulmonary assessment, we were unable to observe a significant correlation in our data with age at operation, age at exercise or time since operation (using either time since first Fontan operation or time since most recent Fontan operation). This is in contrast to reports of a negative correlation between exercise tolerance and both age at operation and age at time of evaluation (14). This discrepancy could be explained by the predominance of adults in our study, in whom the possibility for ventricular remodeling may be reduced. One study (23) serially measured exercise duration and maximal oxygen uptake in patients after Fontan repair and found no change over 2.2 years.

Influence of anatomy on cardiac function. We did not detect a difference in work load, anaerobic threshold or oxygen consumption between patients with an atriopulmonary connection and those with a valved AV connection. The lack of an observed difference may be related to the small number of patients in the study. Other clinical studies have compared patients with nonvalved atriopulmonary connections with those in whom the subpulmonary ventricle is included by a valved connection. No differences were found in peak work load (17), survival or functional class (24). One study (14) observed a higher exercise tolerance for patients with atriopulmonary connection than for patients with the right ventricle within the circuit; however, the effect of a greater proportion of older patients in the latter group may have confounded this result.

Summary. We observed a reduction in objective measures of cardiac function present late after the Fontan operation, which is significantly worse than the subjective clinical assessment of these patients. This observed contrast highlights the difficulty that physicians caring for the adult after the Fontan operation may have in judging the capacity of these patients unless objective and comprehensive exercise data are also utilized in their evaluation.

We acknowledge the technical assistance of Andre Laprade in obtaining the exercise physiology data.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26: 140–8.
2. Fontan F, Deville C, Quaegebeur J, et al. Repair of tricuspid atresia in 100 patients. J Thorac Cardiovasc Surg 1983;85:647–60.
3. Kirklin JK, Blackstone EH, Kirklin JW, Pacifico AD, Bargeron LM. The Fontan operation. Ventricular hypertrophy, age, and data of operation as risk factors. J Thorac Cardiovasc Surg 1986;92:1049–64.
4. Fontan F, Kirklin JW, Fernandez G, et al. Outcome after a "perfect" Fontan operation. Circulation 1990;81:1520–36.
5. Mair DD, Hagler DJ, Puga FJ, Schaff HV, Danielson GK. Fontan operation in 176 patients with tricuspid atresia. Results and a proposed new index for patient selection. Circulation 1990;82 Suppl IV:IV-164–9.
6. Mair DD, Hagler DJ, Julsrud PR, Puga FJ, Schaff HV, Danielson GK. Early and late results of the modified Fontan procedure for double-inlet left ventricle: the Mayo clinic experience. J Am Coll Cardiol 1991;18:1727–32.
7. Driscoll DJ, Offord KP, Feldt RH, Schaff HV, Puga FJ, Danielson GK. Five- to fifteen-year follow-up after Fontan operation. Circulation 1992;85:469–96.
8. Mair DD, Puga FJ, Danielson GK. Late functional status of survivors of the Fontan procedure performed during the 1970s. Circulation 1992;86 Suppl II:II-106–9.
9. Akagi T, Benson LN, Green M, et al. Ventricular performance before and after Fontan repair for univentricular atrioventricular connection: angiographic and radionuclide assessment. J Am Coll Cardiol 1992;20:920–6.
10. Parikh SR, Hurwitz RA, Caldwell RL, Girod DA. Ventricular function in the single ventricle before and after Fontan surgery. Am J Cardiol 1991;67: 1390–5.
11. Ben Schachar G, Fuhrman BP, Wang Y, Lucas RV, Lock JE. Rest and exercise hemodynamics after the Fontan procedure. Circulation 1982;65: 1043–8.
12. Peterson RJ, Franch RH, Fajman WA, Jennings JG, Jones RH. Noninvasive determination of exercise cardiac function following Fontan operation. J Thorac Cardiovasc Surg 1984;88:263–72.
13. Del Torso S, Kelly MJ, Kalff V, Venables AW. Radionuclide assessment of ventricular contraction at rest and during exercise following the Fontan procedure for either tricuspid atresia or single ventricle. Am J Cardiol 1985;55:1127–32.
14. Driscoll DJ, Danielson GK, Puga FJ, Schaff HV, Heise CT, Staats BA. Exercise tolerance and cardiorespiratory response to exercise after the Fontan operation for tricuspid atresia or functional single ventricle. J Am Coll Cardiol 1986;7:1087–94.
15. Zellers TM, Driscoll DJ, Mottram CD, Puga FJ, Schaff HV, Danielson GK. Exercise tolerance and cardiorespiratory response to exercise before and after the Fontan operation. Mayo Clin Proc 1989;64:1489–97.
16. Gewillig MH, Lundstrom UR, Bull C, Wyse RKH, Deanfield JE. Exercise responses in patients with congenital heart disease after Fontan repair: patterns and determinants of performance. J Am Coll Cardiol 1990;15:1424–32.
17. Rhodes J, Garofano RP, Bowman FO, Grant GP, Bierman FZ, Gersony WM. Effect of right ventricular anatomy on the cardiopulmonary response to exercise. Implications for the Fontan procedure. Circulation 1990;81:1811–7.
18. Humes RA, Mair DD, Porter CJ, Puga FJ, Schaff HV, Danielson GK. Results of the modified Fontan operation in adults. Am J Cardiol 1988;61: 602–4.
19. Campeau L. Grading of angina pectoris [letter]. Circulation 1976;54:522–3.
20. Weber KT, Kinasewitz GT, Janicki JS, Fishman AP. Oxygen utilization and ventilation during exercise in patients with chronic cardiac failure. Circulation 1982;65:1213–23.
21. Nakazawa M, Katayama H, Imai Y, et al. A quantitative analysis of hemodynamic effects of the right ventricle included in the circulation of the Fontan procedure. Circulation 1991;83:822–6.
22. Choussat A, Fontan F, Besse P, et al. Selection criteria for Fontan's procedure. In: Anderson RH, Shinebourne EA, editors. Paediatric Cardiology. Edinburgh: Churchill Livingstone, 1978:559–66.
23. Nir A, Driscoll DJ, Mottram CD, et al. Cardiorespiratory response to exercise after the Fontan operation: a serial study. J Am Coll Cardiol 1993;22:216–20.
24. Lee C, Schaff HV, Danielson GK, Puga FJ, Driscoll DJ. Comparison of atriopulmonary versus atrioventricular connections for modified Fontan/ Kreutzer repair of tricuspid valve atresia. J Thorac Cardiovasc Surg 1986; 92:1038–48.